charge deposit account No. 13-2546, in the name of Medtronic, Inc., the fee under 37 C.F.R. §1.17(c) for a three-month extension of time.

In response to the Office Action dated September 27, 2000, Paper No. 3, please amend this application as follows:

In the Claims

1. (Amended 1X) An implantable medical device comprising a body portion overlaid by a fabric overlayer, the body portion comprising [a] at least one polymer intimately mixed with at least one [constituent material in intimate contact with a] therapeutic agent, wherein the therapeutic agent is capable of being released from the body portion of the device.

21. (Amended 1X) A heart valve prosthesis comprising a sewing ring comprising a body portion comprising a biostable polymer intimately mixed [in intimate contact] with a therapeutic agent, said body portion overlayed by a polyester fabric overlayer.

25. (Amended 1X) A heart valve prosthesis comprising a sewing ring comprising a body portion comprising a polymer intimately mixed [metal or metal alloy in intimate contact] with a therapeutic agent, said body portion overlayed by a polyester fabric overlayer.

29. (Amended 1X) In a bioprosthetic heart valve comprising a polymer insert containing struts attached to tissue leaflets to form a valve housing, wherein a fabric sheath encloses the polymer insert to form sewing ring, said sewing ring attached circumferentially to the base of the valve housing, the improvement comprising an releasable therapeutic agent polymer intimately mixed [in intimate contact] with the polymer insert.

37. (Amended 1X) In a mechanical heart valve comprising a metallic ringed valve housing containing a central metallic strut along which a flow occluder disk moves, wherein a fabric sheath encloses a metal insert to form a sewing ring, the improvement comprising a releasable therapeutic

agent intimately mixed with at least one polymer added to the sewing ring [in intimate contact with the constituent material of the insert].

41. (Amended 1X) An annuloplasty ring comprising a body portion overlaid by a polyester fabric overlayer, the body portion comprising a biostable polymer intimately mixed [in intimate contact] with an releasable therapeutic agent.

52. (Amended 1X) A method for ameliorating the inflammatory response associated with heart valve replacement in a patient comprising implanting a prosthetic heart valve into the patient, wherein the prosthetic heart valve comprises a sewing ring comprising a body portion comprising a polymer intimately mixed [constituent material in intimate contact] with a releasable anti-inflammatory agent, said body portion overlayed by a fabric overlayer.

56. (Amended X) A method for ameliorating the inflammatory response associated with heart valve repair in a patient comprising implanting an annuloplasty ring into the patient, wherein the annuloplasty ring comprises a body portion comprising an biostable polymer intimately mixed [in intimate contact] with a releasable anti-inflammatory agent, said body portion overlaid by a fabric overlayer.

60. (Amended 1X) A method of making a medical sewing ring comprising:

incorporating a therapeutic agent into an annular insert comprising a constituent material, such that the therapeutic agent is intimately mixed [in intimate contact] with the constituent material;

enclosing the annular insert in a fabric sheath.

Remarks Regarding the Amendments

Claim 1, 21, 25, 29, 37, 41, 52, 56, and 60 have been amended to

indicate that at least one polymer of the body of the device is intimately mixed with at least one therapeutic agent. The amendment indicates specifically how the previously claimed therapeutic agent is in intimate contact with the therapeutic agent.

Support for amendments of Claims 1, 21, 25, 29, 37, 41, 52 can be found in the specification as indicated below:

> In one embodiment, a polymer of the body portion of the device and a therapeutic agent are intimately mixed either by blending or using a solvent in which they are both soluble (e.g., xylene for silicone and dexamethasone phosphate). This mixture can then be formed into the desired shape and incorporated into the medical device or coated onto an underlying structure of the medical device (p.30, l.11-16)

Applicants respectfully direct the examiner's attention to MPEP where it is stated that:

> "Obviously, however, the failure to provide explicit antecedent basis for terms does not always render a claim indefinite. If the scope of a claim would be reasonably ascertainable by those skilled in the art, then the claim is not indefinite. Ex parte Porter 25 USPQ2d 1144, 1145 (Bd. Pat. App. & Inter. 1992). Inherent components of elements recited have antecedent basis in the recitation of the components themselves. For example, the limitation "the outer surface of said sphere" would not require an antecedent recitation that the sphere has an outer surface." MPEP §2173.05(e)

Remarks Following Examination

Rejection of Claims 35 and 36 Under 35 USC § 112, Second Paragraph

Claims 35-36 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the examiner rejected claim 35 (thereby dependent claim 36) as having insufficient basis in the specification for the recitation of the "flow

occluder." Applicants respectfully traverse.

The test for compliance under §112, second paragraph has been defined in case law to consist of two requirements under the statute: (1) whether the applicant has stated the invention as something elsewhere in the application which would not fall under the scope of the claims; and (2) whether the claims would be communicated with a reasonable degree of particularity and distinctness to a person skilled in the art in light of the content of the disclosure and the teachings of the prior art. MPEP §2171, §2173, and §2173.02.

Applicants respectfully indicate that the present application defines sufficiently for one skilled in the art the term "flow occluder" of claim 35. The applicants direct the examiner's attention to the following locations in the specification for reference to the flow occluder:

> "Mechanical valves are valves made on non-biological materials, consisting of a valve housing, a flow occluder, and a sewing ring. Bioprosthetic valves are composed of housing (known as a stent), a flow occluder (usually pericardium or aortic root tissue from animal sources that has been chemically preserved) and sewing ring." (p.2, l.13, emphasis added)
>
> "Figure 2 is a more detailed illustration of a bioprosthetic heart valve embodying the present invention. Bioprosthetic valve 30 contains three tissue leaflets 26, which together function as a flow occluder." (p.23, l.17, emphasis added)
>
> "Figure 3 is a more detailed illustration of a mechanical heart valve embodying the present invention. Mechanical valve 40 comprises a metallic ringed valve housing 42 containing a central metallic strut 44 along which the flow occluder disk 46 moves." (starting at p.24, l. 27, emphasis added)

As noted above, applicants' specification specifically describes and illustrates a "flow occluder" and its relation to mechanical heart valves. Further, the flow occluder of a mechanical heart valve is well recognized in

the art. Applicants refer the examiner to the Tweden reference, cited by the examiner, at 14 having a flow occluder.

The applicants respectfully indicate that use of the term "flow occluder" is distinctly defined in the specification and is a well known component of heart valves, thereby meeting the requirements under 112, second paragraph. Applicants respectfully request the present rejection to claims 35-36 be removed.

Rejection of Claims 37-38 under 35 USC § 112, Second Paragraph.

The examiner also rejected Claim 37 (thereby dependent claims 38-44) under §112, second paragraph, alleging that there was no antecedent basis for the "constituent material of the insert." Applicants respectfully contend that this rejection has been rendered moot by the submitted amendments.

However, applicants wish to point out the use of the term "constituent material" is adequately supported by the specification as follows:

> "To do this, the present invention does not involve modifying the chemistries of the constituent materials of the devices, rather it involves using anti-inflammatory agents as biological response modulators to control the host's response to the constituent materials." (starting at p. 11, l. 5, emphasis added)
>
> "The body portion is not limited to any particular constituent material, and it can be porous or nonporous, biodegradable or biostable, flexible or inflexible, as indicated by the intended use." (p.13, l. 5. – emphasis added)
>
> "The constituent material of the body portion of the implantable device is in intimate contact with a therapeutic agent, such as a steroidal or nonsteroidal anti-inflammatory agent, that controls, reduces or attenuates the body's inflammatory response to the implanted medical device, and which is capable of eluting through the fabric overlayer." (p.13., l.25. – emphasis added).
>
> "To this end, the present invention provides an implantable

medical device having a body portion comprising a constituent material in intimate contact with a therapeutic agent, such as an anti-inflammatory agent, the body portion overlayed by a porous fabric." (p.19, l. 3 – emphasis added)

"The body portion of an implantable medical device of the invention can be fabricated from any desired constituent material or materials, without limitation. Preferably, the constituent material of the body portion of the device is biocompatible. The choice of constituent material will depend on the intended structure and function of the device." (p.26., l 18. – emphasis added)

"The constituent material of the body portion of an implantable medical device of the invention is in intimate contact with one or more therapeutic agents (also referred to herein as simply "drugs"), and the body portion is fabricated such that the therapeutic agent can elute away from its surface and ultimately through the porous fabric overlayer." (p.28, l.5. – emphasis added)

"Any means by which the therapeutic agent can be incorporated into the medical device such that it is in intimate contact with a constituent material of the body portion of the device are within the scope of the present invention." (p. 28.,l.26, emphasis added)

Claim Rejections Under 35 USC § 102 In View of Tweden

Claims 1-8, 12, 14, 15-17, 18-22, 24-26, 28-30, 34, 35-37, 38, 41, 42, 44-49, 52, 53, 55-57, 59, 60-66, 69-71, and 72 were rejected under 35 U.S.C. 102(b) as being anticipated by Tweden et al., U.S. Patent No. 5,895,419 (herein referred to as Tweden).

The examiner cites Tweden for disclosing an implantable medical device at 22 with a fabric overlayer at 24. The examiner indicates that it is "implied" that the device may be coated with therapeutic agents by reference to column 4, lines 21-22 of the patent. Several other locations of

the Tweden reference are held to disclose specific aspects of the invention.[1] Applicants agree that Tweden shows the features of a mechanical heart valve, however, strongly traverse that Tweden adequately implies that the device may be coated with a therapeutic agent.

Applicants submit that the Tweden reference describes a method for providing a metallic coating on fabric portions of a prosthesis, the preferred metal being silver. The silver coating is applied to the fabric surface in order to make it more biocompatible.[2]

Tweden describes three ways to provide the silver coating:

> "First, the fabric used in the construction of the devices may be coated after the fabric is formed. Second, the yarn or fiber that makes up the fabric can be coated before the fabric is formed. Third, after the fabric portion is constructed, the fabric portion itself may be coated with the silver. In addition, the silver coating may be applied directly to a device." (Col. 2, l. 52-58).

Further, Tweden only contemplates the application of the silver coatings by vapor-deposition or by sputtering, or other techniques:

> "For instance, the silver coatings may be applied by vapor-deposition or by sputtering. The use of the vapor-deposition technique is described in U.S. Pat. No. 4,167,045 to Sawyer. Although any of a number of techniques can be used to create

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[1] (1) With regard to claims 2-5, 22, 30, 37, 42, 47, 63, the constituent material comprising a polymer at column 3, line 36, and in particular, silicone column 3, line 38; (2) With regard to claims 6-8, 53, 57, 62, 66 the polymer fiber being polyethylene is disclosed at column 3, line 37, and the polymer fiber being polyester or polyethylene terephthalate disclosed at column 5, lines 34-35; (3) With regard to claims 12, 34, 44, and 69, the antimicrobial agent is disclosed at column 4, line 22; (4) With regard to claims 14, 15, 17, the therapeutic agent being coated on or compounded into the body portion of the device is disclosed at column 4, lines 32-39: (5) With regard to claim 21, a sewing ring is closed at 66; (6) With regard to claims 25, 28, 35, 36, a heart valve prosthesis is disclosed at 10, and it is disclosed that the heart valve may be bioprosthetic or mechanical, at column 2, lines 3-6, and lines 30-35; (7) With regard to claims 26, 38, 48, 49, 64,and 65, the body portion comprising metal, titanium in particular, is disclosed at column 3, line 40; (8) With regard to claim 35, an occluder is disclosed at column 2, line 32; (9) With regard to claim 37, a flow occluder disk is disclosed at 14; (10) With regard to claim 41, an annuloplasty ring is disclosed at 22; (11) With regard to claim 45, a sewing ring is disclosed at 66.

[2] U.S. Patent No. 5,895,419, Abstract.

> the silver coating, it is important that the coating be extremely adherent to the fabric or other materials to prevent excessive circulation of the cytotoxic silver material throughout the body, while retaining porosity necessary for tissue ingrowth." (col. 4, l. 39-48)

No other methods of application of the silver coating seem to appear in the specification. Tweden only makes one passing reference to coating with other agents, in reference to a passive assist device:

> "Device 60 [passive assist device] may be coated with materials including silver or other antimicrobial metals, peptides, and sulfonated hydrogels. (Col 4, l. 20-22 - emphasis added)

Based on this one sentence in the Tweden reference, the examiner rejected claims 1-8, 12, 14, 15-17, 18-22, 24-26, 28-30, 34, 35-37, 38, 41, 42, 44-49, 52, 53, 55-57, 59, 60-66, 69-71, and 72.

To be an anticipatory reference of the claimed invention, a reference must contain sufficient technical information to describe the claimed invention to a person of ordinary skill in the art to which the claimed invention pertains and to enable a person to make and use the claimed subject matter, without first having to perform extensive experimentation or make an unobvious contribution.

Consistent with the allowed claims[3] in Tweden, the Tweden reference essentially relates to metallic coatings of the fabric portion of a heart prosthesis and provides methods and examples of such coatings. Tweden only mentions tangentially in one sentence that one can coat the device (which would include the fabric portion) with other antimicrobial metals, peptides, or hydrogels, but completely fails to disclose how such agents are coated onto the device. Presumably, this would be accomplished

[3] 1. An implantable heart prosthesis, said prosthesis comprising:
an orifice ring having an outer periphery and an inner periphery, said ring defining an annulus;
said annulus defining a passage for the flow of blood;
a fabric member coupled to at least said outer periphery of said orifice ring and adapted for coupling to a patient's heart tissue for an extended duration;
said fabric member carrying silver to thereby substantially inhibit microbial growth on the fabric member.

by applying the teachings for coating fabrics, i.e., applied by vapor-deposition or by sputtering. Assuming arguendo that one can apply therapeutic substance by these techniques, one would fail to achieve an intimate mixing of the therapeutic agent and at least one polymer contained in the body of the device.

Further, it is important to note that the coatings of Tweden are applied in such a way that they are "extremely adhesive so that materials do not enter into the circulation to prevent cytotoxicity."[4] Reading Tweden as a whole, Tweden would most likely permanently attach the therapeutic agent to the device by applying an external coating to the fabric. Such a teaching is away from the purpose of applicants' invention to release therapeutic substances from devices having a body member with a fabric overlay. Tweden does not teach having at least one therapeutic substance intimately mixed with at least one polymer incorporated into the body member of the device nor does it teach the incorporation of the therapeutic agent in the materials of the body member such that it is released into the circulation.

In view of applicants amendments of independent claims 1, 21, 25, 29, 37, 41, 45, 52, 56, 60, and arguments submitted above, applicants respectively request removal of the rejection under 35 U.S.C. § 102.

Claim Rejections Under 35 USC § 103

Tweden in view of Fearnot

Claims 9-11, 23, 27, 32, 33, 39, 40, 43, 50, 51, 54, 58, 67, and 68 were rejected under 35 USC 103(a) as being unpatentable over Tweden et al., 5,895,419, in view of Fearnot et al., 5,609,629 (herein referred to as Fearnot). The examiner has pointed to the fact that Tweden does not disclose the threapuetic agent being an anti-inflammatory agent, or in particular, dexamethasone. However, the examiner uses Fearnot for suggesting a layer of dexamethasone can be coated on an implantable

[4] US Patent No. 5,895,419, Col. 4, lines 43-48

medical device for implantation into, for example, the vascular system (see column 4, line 33). The examiner thus argues that it would have been obvious to one of ordinary skill in the art at the time the invention was made, to apply a layer of dexamethasone onto an implantable medical device, such as the Tweden heart valve, and use a known therapeutic agent as taught by Fearnot for use with a medical device for implantation into the vascular system. Applicants respectfully traverse.

Applicants contend that the examiner has not established a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, the examiner must show:

1) that the prior art references relied upon teach or suggest all the claim limitations;

2) some suggestion or motivation to modify or combine information in the prior art or pool of knowledge available to one of ordinary skill art at the time of filing the application; and

3) a reasonable expectation of success in modifying or combining the prior art teachings.

In re Fine, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988), citing In re Lalu, 747 F.2d 703, 705, 223 U.S.P.Q. 1257, 1258 (Fed. Cir. 1984). "Obviousness is tested by what the combined teachings of the references would have suggested to those of ordinary skill in the art." In re Fine, at 1599, citing In re Keller, 642 F.2d 413, 425, 208 U.S.P.Q. 871, 881 (C.C.P.A. 1981). Prior art references do not establish obviousness "absent some teaching or suggestion supporting the combination." ACS HosD. Svs.. Inc. v.Montefiore Hosp., 732 F.2d 1572, 1577, 221 U.S.P.Q. 929, 933 (Fed. Cir. 1984).

First, applicants indicate that Tweden taken in view of Fearnot does not teach or suggest all the claim limitations. As previously discussed in the previous section, Tweden fails to teach one skilled in the art how to make a releasable therapeutic agent intimately mixed with at least one

polymer incorporated into the device (assuming arguendo, that the methods of Tweden can be applied to therapeutic agents – see prior arguments under 102). Tweden is primarily directed to impregnating the fabric overlayer cloth with silver. Even assuming that the body of the device can be coated, Tweden teaches away from a releasable therapeutic agent as claimed nor provides the methods for achieve the claimed limitation of having an intimately mixed therapeutic agent and polymer in the body of the device.

Fearnot teaches a coated medical device with a releasable bioactive layer; however, the release mechanism is accomplished by adding a porous coating layer positioned over a bioactive layer. Applying Tweden in view of Fearnot, one would arrive at a different device for achieving release of a therapeutic agent. The present invention differs from the combined teaching of Tweden and Fearnot in that polymers of the device are intimately mixed with the therapeutic agent(s).

Applicants further maintain that neither Tweden nor Fearnot provide a suggestion or motivation to combine their teachings to produce Applicants' invention. As such, the two references cannot properly be combined. Further, applicants also have demonstrated that even if the references are combined there is no expectation of success in obtaining the claimed invention.

In summary, applicants assert that the combination of Tweden and Fearnot does not establish a prima facie case of obviousness because:

1) the combination does not teach or suggest all the claim limitations,

2) neither provides a reasonable expectation of success in modifying or combining the publications, and

3) neither contains motivation or suggestion to combine the publications.

In view of applicants amended claims and arguments, they respectfully request the present rejection under 35 U.S.C. §103 be removed.

Tweden in View of Chanda

Claim 13 was rejected under 35 U.S.C. 103(a) as being unpatentable over Tweden et al., 5,895,419, in view of Chanda et al., 5,645,587. The examiner found that Tweden substantially discloses the claimed invention, but does not disclose the antimicrobial agent as being gentamicin or rafampicin. However, the examiner uses the teaching of Chanda for the use of heparin after neutralization with gentamicin as essential in prevention of calcification in tissue grafts, which is the main cause of failure of bioprosthetic heart valves (see column 3, lines 45-47, and lines 61-62). Thus, the examiner contends that it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide a gentamicin in combination with heparin on the Tweden heart valve in order to prevent calcification.

First, applicants indicate that Tweden taken in view of Chanda does not teach or suggest all the claim limitations. As previously discussed in the previous sections, Tweden fails to teach one skilled in the art how to make a releasable therapeutic agent intimately mixed with at least one polymer incorporated into the device.

Chanda describes biotissue grafts formed by covalent binding of heparin to glutaraldehyde-treated xenografts of heterografts to prevent calcification or thrombosis formation. The xenograft or heterografts are prepared by first treating the tissues with glutaraldehyde. Subsequently the tissues are reacted with the amino compound chitosan. After that the

unreacted aldehyde groups are then neutralized by treating with glycine-gentamicin. Finally, the free aldehyde moieties of partially degraded heparin are used to covalently bind the free amino groups of chitosan and gentamicin.

Combination of Tweden and Chanda is not even possible because there is no common starting point. Chanda describes modification of biological tissue valves, whereas Tweden describes modification of the mechanical ring and cloth overlayer. Combining the Tweden in view of Chanda, one would end up with a sewing ring of Tweden containing the chemically modified tissue valve of Chanda. This is not the claimed invention.

Applicants further maintain that neither Tweden nor Chanda provide suggestion or motivation to combine their teachings to produce applicants' invention. As such, the two references cannot properly be combined. Further, applicants also have demonstrated that even if the references are combined there is no expectation of success in obtaining the claimed invention.

In summary, applicants assert that the combination of Tweden and Chanda does not establish a prima facie case of obviousness. In view of applicants amended claims and arguments, they respectfully request that the present rejection under 35 U.S.C. §103 be removed.

Tweden In View of Myers

Claim 31 was rejected under 35 U.S.C. 103(a) as being unpatentable over Tweden et al., 5,895,419, in view of Myers, 5,716,397. The examiner has found that Tweden discloses the invention substantially as found in

claim 1, however, Tweden does not disclose a polymer insert comprising radio-opaque flexible silicone rubber. Myers discloses an annuloplasty ring consisting of a soft core of silicone rubber impregnated with radiopaque salt. Thus, it would have been obvious, the examiner contends to one of ordinary skill in the art at the time the invention was made to use the radio-opaque silicone rubber as polymer insert as an annuloplasty ring along with the coated device.

First, applicants indicate that Tweden taken in view of Chanda does not teach or suggest all the claim limitations. As previously discussed in the previous sections, Tweden fails to teach one skilled in the art how to make a releasable therapeutic agent intimately mixed with at least one polymer incorporated into the device.

Myers adds nothing further to make applicants invention obvious. Myers is directed to a flexible stiffening ring that is used during annuloplasty for heart valve repair. The stiffening ring can then be withdrawn once the annuloplasty ring is in place. In one sentence in the discussion of the background of the invention, it is mentioned that annuloplasty rings are known to consist of a soft core of silicone rubber impregnated with a radio-opaque salt, e.g., barium sulfate (col. 1, l. 46-49), but there is no reference to this teaching.[5]

Even in view of the inadequacy of the reference, applicants indicate that using the teaching of the general structure of the heart valve by Tweden, and the teaching of Myers for use of impregnating silicone with barium sulfate, one does not arrive at applicants' invention. First, barium

[5] Checking the next mentioned reference, US Patent No. 5,011,481, added no further information regarding use of the radionuclide salt.

sulfate is used as a radionuclide, not a therapeutic agent as claimed. It used for imaging, but has no general therapeutic value. Second, the silicone is impregnated, versus achieving a polymer intimately mixed with the therapeutic agent.

Applicants further maintain that neither Tweden nor Myers provide suggestion or motivation to combine their teachings to produce applicants' invention. As such, the two references cannot properly be combined. Further, applicants also have demonstrated that even if the references are combined there is no expectation of success in obtaining the claimed in invention.

In summary, applicants assert that the combination of Tweden and Myers does not establish a prima facie case of obviousness . In view of applicants amended claims and arguments, they respectfully request that the present rejection under 35 U.S.C. §103 be removed.

Tweden In View of One Skilled In The Art

Claim 73-75 were rejected under 35 U.S.C. 103(a) as being unpatentable over Tweden. Tweden was found by the examiner to disclose the invention substantially as claimed with respect to claim 1, except that Tweden does not disclose an implantable infusion pump with a polyester pouch surrounding the pump, and a constituent material in intimate contact with an anti-inflammatory agent. However, the examiner contends that it would have been obvious to one of ordinary skill in the art at the time of the invention to use a polyester outer layer surrounding a metal or polymer frame with an implantable pump, as the materials were known in implantable devices, such as a heart valve disclosed by Tweden (see column 3, lines 30-36). Moreover, the examiner cites Fearnot for the

proposition that it would have obvious to apply a layer of dexamethasone onto an implantable medical device, as a known therapeutic agent for use with a medical device for implantation.

The examiner has suggested that with the teachings of the heart valve of Tweden, one skilled in the art would know to use a polyester outer layer surrounding a metal or polymer frame with an implantable pump because the materials were known in implantable devices. Applicants assert this does not even make a threshold argument. If the examiner is providing his personal knowledge as to what is known to those skilled in the art, the applicants request that the examiner submit an affidavit to that effect on the record, for it to be duly considered. MPEP 2144.03; see also 37 CFR 1.104(d)(2).

Further the level of skill in the art cannot be relied upon to provide the suggestion to combine references. Al-Site Corp. V. VSI Int'l., 174 F.3d 1308, 50 USPQ2d 1161 (Fed Cir. 1999); MPEP 2143.01. As such, it is improper to use the examiner's knowledge of one skilled in the art as motivation for the combination. Further, applicants suggest that Tweden, in view of the knowledge of one skilled in the art, there is no expectation of success in obtaining the claimed in invention.

In summary, applicants assert that the combination of Tweden and the knowledge of one skilled in the art does not establish a *prima facie* case of obviousness . In view of applicants amended claims and arguments, they respectfully request thatthe present rejection under 35 U.S.C. §103 be removed.